Non-invasive ventilation 2

Ventilatory support after extubation in critically ill patients

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This is the second in a Series of two papers about non-invasive ventilation

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The periextubation period represents a crucial moment in the management of critically ill patients. Extubation failure, defined as the need for reintubation within 2–7 days after a planned extubation, is associated with prolonged mechanical ventilation, increased incidence of ventilator-associated pneumonia, longer intensive care unit and hospital stays, and increased mortality. Conventional oxygen therapy is commonly used after extubation. Additional methods of non-invasive respiratory support, such as non-invasive ventilation and high-flow nasal therapy, can be used to avoid reintubation. The aim of this Review is to describe the pathophysiological mechanisms of postextubation respiratory failure and the available techniques and strategies of respiratory support to avoid reintubation. We summarise and discuss the available evidence supporting the use of these strategies to achieve a tailored therapy for an individual patient at the bedside.

Introduction

The peri-extubation period represents a crucial moment in the management of critically ill patients. Postextubation acute respiratory failure (ARF) occurs in 10–20% of patients who meet all weaning criteria and successfully perform a spontaneous breathing trial, who might require emergency reintubation.[1,2] Reintubation is usually related to airway failure (aspiration, ineffective cough, or upper airway obstruction), weaning failure (primary respiratory failure, congestive heart failure, onset of new sepsis, acute coronary syndrome, or neurological impairment), or surgical complications such as bleeding or anastomotic leak.[3] In particular, surgical complications are a major cause of extubation failure in the postoperative setting, needing prompt identification and correction.

Extubation failure has been defined as the need for reintubation occurring within 2–7 days after a planned extubation,[1,3] resulting in increased mortality (25–50%), prolonged mechanical ventilation, increased frequency of ventilator-associated pneumonia, and longer intensive care unit (ICU) and hospital stays.[4–7] It is therefore essential to identify patients at high risk of postextubation ARF in order to choose an appropriate strategy of respiratory support able to improve their outcome.

Conventional oxygen therapy (COT) is commonly used to correct residual oxygenation impairment after extubation, a condition reported as a frequent cause of weaning failure.[8,9] Although COT can improve oxygenation, it has only a minimal effect on the main pathophysiological mechanisms which can lead to postextubation ARF and reintubation (eg, atelectasis, excessively high respiratory workload, or decreased respiratory muscle force). Non-invasive ventilation (NIV) and high-flow nasal therapy (HFNT) have been implemented as effective alternative approaches aimed at protecting extubation.[10–12]

In this Review we will describe: the pathophysiological mechanisms of postextubation ARF, the main techniques of non-invasive respiratory support used after extubation (NIV, HFNT, and COT), strategies of postextubation respiratory support (facilitative, preventive, and therapeutic) and their indications to achieve a tailored therapy for specific types of patient, and areas of uncertainty and of future research.

Key messages

- Extubation failure is associated with prolonged mechanical ventilation, increased frequency of ventilator-associated pneumonia, longer stays in the intensive care unit and in the hospital, and increased mortality
- Identifying patients at greater risk of extubation failure is important for choosing the appropriate technique of non-invasive ventilatory support to improve weaning outcome
- Several techniques of respiratory support (conventional oxygen therapy, high-flow nasal therapy, continuous positive airway pressure, and non-invasive ventilation) can be used with different strategies (facilitative, preventive, or therapeutic) to avoid extubation failure
- Any postextubation respiratory support treatment should not delay intubation and escalation to invasive mechanical ventilation, when this is more appropriate
- In the era of precision medicine and personalisation of care, future studies are needed to help clinicians to use the right device, with the right setting, in the right patient, at the right time

Pathophysiological changes related to extubation

Extubation and the subsequent passage from positive pressure mechanical ventilation to unassisted breathing are the cause of several pathophysiological changes in the airway status or in the weaning (cardiorespiratory) status, including lung aeration, haemodynamics, and neuromuscular function, which, alone or in association, are the substrate for extubation failure, especially in high-risk patients (figure 1).

Changes in airway status

Upper airway obstruction is one of the common causes of extubation failure (2–16% of ICU patients), requiring, in

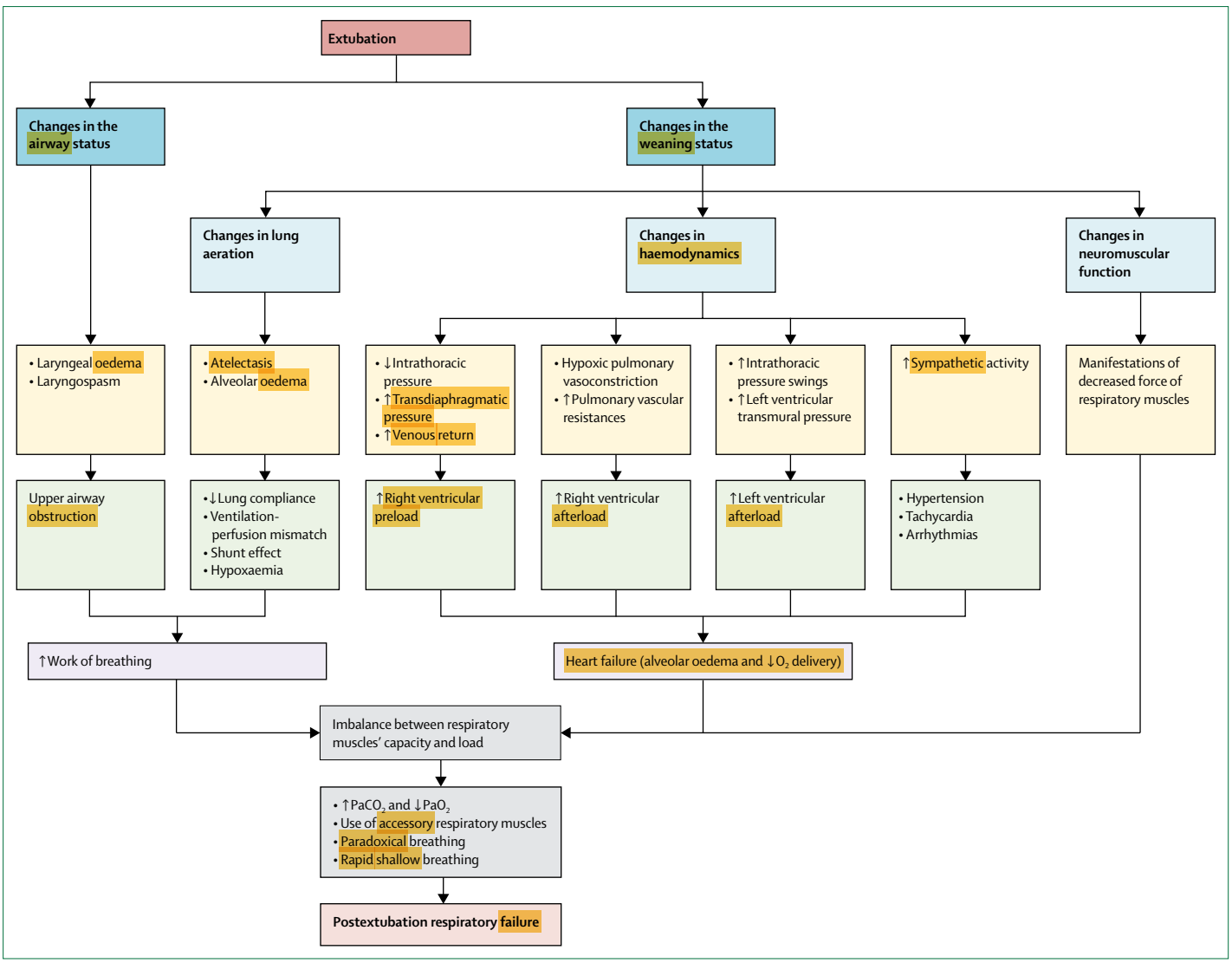

***Figure 1*: Pathophysiological changes in the airway and weaning status occurring after extubation and their linkage with postextubation respiratory failure**
PaO_2=arterial partial pressure of oxygen. $PaCO_2$=arterial partial pressure of blood carbon dioxide.

some cases, an emergent reintubation.[13] The most frequent cause of upper airway obstruction after extubation is laryngeal oedema, which derives from mechanical trauma caused by the intubation, especially in cases of difficult intubation, multiple intubation attempts, prolonged intubation, use of inappropriately large endotracheal tube size, high cuff pressure, female sex, and reintubation after unplanned extubation. After removal of the endotracheal tube, the airway diameter might be substantially reduced, thus increasing airway resistance, which, in turn, can lead to respiratory distress.[13–15] The quantitative cuff leak test is a screening test recommended before extubation in patients at risk of postextubation stridor.[16] The test is considered positive when the cuff leak volume (which is the difference between expiratory volume with inflated cuff and expiratory volume when the cuff is deflated) is less than 130 mL or if the expiratory volume with deflated cuff is less than 12% of the inspiratory volume. In these cases, the administration of steroids, at least 4 h before extubation, might decrease laryngeal inflammation and oedema.[12,13,17] Another less frequent cause of upper airway obstruction is represented by laryngospasm due to a greater susceptibility of inflamed airway to reflexogenic stimuli, such as epipharyngeal and laryngopharyngeal stimulation.

Additionally, excessive tracheobronchial secretions at the time of extubation, together with a weak or ineffective cough, can lead to impaired airway competency and, consequently, to extubation failure.

Changes in weaning status

Weaning status includes lung aeration, haemodynamics, and neuromuscular function. Discontinuation of

mechanical ventilation might cause a loss of pulmonary aeration, leading to decreased lung compliance, ventilation–perfusion mismatch, and shunt effect.[18,19] Different pathophysiological changes are associated with loss of lung aeration, such as atelectasis, alveolar transudation, and oedema. During spontaneous breathing, the decrease in transpulmonary end-expiratory pressure can reduce lung volume to values below the closing capacity in unstable alveoli, resulting in collapse and atelectasis formation. Atelectasis plays a fundamental role in the pathophysiology of postextubation ARF because the heterogeneity of the lung parenchyma can lead to elevated regional driving transpulmonary pressure (the difference between end-inspiratory transpulmonary pressure and end-expiratory transpulmonary pressure), worsening of lung injury, pulmonary oedema, and respiratory distress.[18,19] Besides, intrapulmonary shunt in atelectatic zones elicits hypoxic pulmonary vasoconstriction, which increases pulmonary vascular resistances. Alveolar transudation and oedema after extubation are caused by increased difference between intravascular capillary pressure and alveolar pressure and by increased cardiac output.

Discontinuation of mechanical ventilation can cause pronounced negative swings in intrathoracic pressure, depending on the patient's inspiratory effort.[18–21] This implies an increase in left ventricular transmural pressure and afterload, which derives from the difference between systolic aortic pressure and intrathoracic pressure. Transdiaphragmatic pressure (the difference between abdominal pressure and intrathoracic pressure) increases after discontinuation of ventilation because there is a greater diaphragmatic excursion during spontaneous breathing than during mechanical ventilation, causing higher abdominal pressure and a compressive effect on the abdominal viscera and vessels, while intrathoracic pressure decreases to negative values. This pressure gradient leads to an increase in venous return and in right ventricular preload. In addition, at extubation, stimulation of airway receptors causes increased sympathetic activity, which might result in hypertension, increased heart rate, and arrhythmias.[22,23]

Liberation from mechanical ventilation requires adequate neuromuscular activity to overcome the impedance of the respiratory system, to meet metabolic demands, and to maintain adequate gas exchanges.[1] Mechanical ventilation can be associated with diaphragmatic weakness, injury, and atrophy, which occur rapidly in critically ill patients, leading to difficult weaning.[24] Diaphragmatic atrophy is associated with excessive ventilatory assistance, which acts on central drive to suppress the patient's inspiratory effort, whereas inadequate ventilatory support potentially causes insufficient unloading of the respiratory muscles, leading to load-induced diaphragmatic inflammation and injury.[25] Other risk factors are related to diaphragmatic dysfunction in critically ill patients, such as primary neuromuscular weakness and critical illness polyneuropathy and myopathy.[26] Several studies have shown that diaphragm dysfunction developing during mechanical ventilation is strongly linked to difficult weaning and worsened clinical outcomes.[25,27–29] During unassisted breathing after extubation, these changes in diaphragm function can lead to an imbalance between the respiratory muscles' capacity and the respiratory load, with clinical manifestations of respiratory distress such as use of accessory respiratory muscles, paradoxical breathing, rapid shallow breathing, and gas exchange impairment.

All these pathophysiological changes can lead to increased work of breathing and CO_2 production, worsening of oxygenation, recruitment of accessory respiratory muscle, paradoxical breathing, rapid-shallow breathing and, thus, a further increase in respiratory load. The imbalance between the available respiratory muscle force and the required muscle power finally results in muscle exhaustion and ARF. Furthermore, hypoxia and metabolic acidosis impair respiratory muscle function and cardiac function, triggering a vicious circle that, in the absence of adequate therapeutic measures, can lead to cardiorespiratory arrest.

Techniques of respiratory support after extubation

Different techniques, such as NIV, HFNT, or COT, are used to support oxygenation or spontaneous ventilation with the aim of protecting extubation. We summarise the main physiological effects of each technique, focusing on the relevant aspects in the postextubation setting.

Non-invasive ventilation

NIV is a form of mechanical ventilatory support that does not require an artificial airway (endotracheal tube or tracheostomy) and is provided through various interfaces (ie, mask, helmet, prongs).[30] The term NIV usually includes both continuous positive airway pressure (CPAP) and non-invasive, bi-level positive pressure ventilation, often delivered with pressure support ventilation and positive end-expiratory pressure.[31] In this Review, we use the term NIV to refer to bi-level positive pressure ventilation, and use the term CPAP to specifically refer to this distinct mode. CPAP delivers a constant positive airway pressure throughout the entire respiratory cycle (both inspiration and expiration), without providing any assistance to the patient's inspiratory effort. NIV is a ventilatory technique in which a positive inspiratory pressure (ie, pressure support ventilation) is provided by the ventilator, assisting the patient's inspiratory effort.[21,30]

In patients without criteria for immediate intubation (eg, inability to protect the airways, cardiorespiratory arrest), NIV offers several advantages compared with invasive mechanical ventilation, including improved patient comfort, reduced sedation need, lower frequency of nosocomial infections, and fewer complications related to the intubation manoeuvre (eg, airway injuries, laryngeal oedema, and glottic oedema).[32–36]

NIV and CPAP have several physiological effects on the respiratory and cardiovascular systems. CPAP and positive end-expiratory pressure prevent airway closure and alveolar collapse at the end of expiration, thus promoting alveolar recruitment, increasing aerated lung volume, decreasing ventilation–perfusion mismatch, and improving hypoxaemia.[21] Application of a pressure above positive end-expiratory pressure (ie, in pressure support ventilation mode) supports the inspiratory phase and increases tidal volume and alveolar ventilation, leading to an improvement in gas exchange.[36,37] NIV also reduces the work of breathing. The inspiratory pressure support decreases indices of diaphragmatic effort and energy expenditure (eg, transdiaphragmatic pressure and pressure–time product, diaphragmatic electric activity).[36,37] The use of positive end-expiratory pressure further reduces the work of breathing by decreasing inspiratory threshold load (in patients with intrinsic positive end-expiratory pressure) and elastic load by increasing respiratory system compliance.[21,38–41] The change in respiratory pattern and reduction of dyspnoea are important clinical effects resulting from gas exchange improvement and from reduction of the patient's inspiratory effort.[36,37] Compared with spontaneous breathing, positive pressure ventilation delivered during NIV and CPAP reduces left ventricular preload, afterload, and compliance in healthy individuals.[21,42,43] These effects can be useful in pathological conditions, such as ARF owing to cardiogenic pulmonary oedema and heart failure, a not-infrequent condition associated with extubation occurring as a consequence of the change in intrathoracic pressure (from positive during mechanical ventilation to negative after extubation) in patients with heart disease (eg, coronary artery disease or mitral valve disease). In this case, the constant positive pressure provided throughout the respiratory cycle with CPAP increases intrathoracic pressure, reduces venous return to the right atrium, and decreases left ventricular transmural pressure (and, accordingly, left ventricular afterload), thus resulting in enhanced left ventricular performance and decreased extravascular lung water.[44] Several studies have shown that, as compared with COT, the application of CPAP and NIV in patients with cardiogenic pulmonary oedema has many beneficial physiological effects, including improvement in respiratory mechanics and gas exchange, decrease in the work of breathing, and reduction of systolic arterial pressure and heart rate,[41,45] which can decrease the need for intubation and improve patient outcomes.[46,47]

High-flow nasal therapy

Clinical efficacy of HFNT is already known in the neonatal and paediatric settings,[48] but in recent years HFNT has been increasingly used in critically ill adults.[10] This device delivers high flow of humidified gas, with a set inspired oxygen fraction (FiO_2) and a set gas flow up to 100 L/min (most commonly 50–60 L/min).[49]

Several physiological effects of HFNT have been described, underlining how it is a technique of true respiratory support, rather than an alternative way to simply deliver oxygen therapy.[48,50–55] First, HFNT is able to deliver a higher and more stable FiO_2. The continuous, high gas flow, in fact, can match or even exceed the patient's inspiratory flow, thus decreasing entrainment of ambient air during inspiration and improving oxygenation.[9,55–59] Second, the high gas flow washes out the upper airway (anatomic) dead space. In a study in ten healthy volunteers, Moller and colleagues[60] showed a direct relationship between gas flow rate and clearance of a radioactive tracer gas in the upper airways, confirming their previous findings in an upper airway model.[61] In three tracheotomised patients, these authors reported flow-dependent FiO_2 increase and reduced inspired carbon dioxide (CO_2) in the trachea, which supports the hypothesis that HFNT decreases rebreathing and dead space, thus improving alveolar ventilation and gas exchange.[60] Third, HFNT generates positive airway pressure. The high gas flow increases expiratory resistance, thus raising upper airway pressure during expiration (positive end-expiratory pressure effect).[54] This effect is dependent on gas flow, mouth opening, and size of the nasal cannula. Studies have shown a positive linear correlation between the set gas flow and the value of mean airway pressure,[49,62] which can reach an average of 3·3 cm H_2O (SD 1) at 50 L/min when the mouth is closed.[62] The higher airway pressure increases the end-expiratory lung volume, promoting alveolar recruitment and preventing alveolar collapse, which improves ventilation:perfusion ratio and oxygenation.[54,55,63]

Another physiological effect of the HFNT is to decrease the patient's inspiratory effort. In a physiological study in patients with acute respiratory failure, Mauri and colleagues reported that, as compared with a standard facial mask, HFNT decreased oesophageal pressure swings (by 19% on average) and pressure–time product, a measure of the metabolic work of breathing (by 28% on average).[55] Several mechanisms might explain the reduction in the patient's inspiratory effort with HFNT, including the decrease in hypoxic drive related to improvement in oxygenation, enhanced CO_2 clearance related to washout of the upper airways, and improvement in lung mechanics. In addition, the high gas flow splints the upper airways, reducing their tendency to collapse. This causes a reduction of inspiratory airway resistance and a lower resistive respiratory work. Finally, HFNT improves humidification of inspired gas, facilitating clearance of secretions through preservation of normal ciliary function of epithelial cells and composition of mucus.[52,64] Moreover, delivery of heated and humidified gas decreases the metabolic cost of breathing associated with gas conditioning.

All these effects contribute to improve patient comfort and alleviate dyspnoea during HFNT.[9,57] As compared with other forms of oxygen therapy and respiratory support delivered through a facial interface, the greater comfort with HFNT is also related to the nasal interface, which

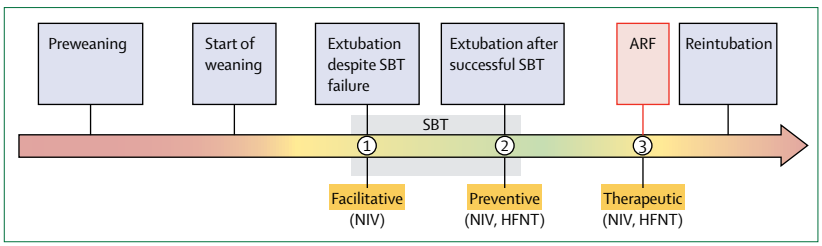

Figure 2: **Strategies of ventilatory support after extubation**
SBT=spontaneous breathing trial. ARF=acute respiratory failure. NIV=non-invasive ventilation. HFNT=high-flow nasal therapy.

	Facilitative	Preventive	Therapeutic
NIV–CPAP*	Suggested in patients with hypercapnic respiratory failure; no recommendation for hypoxaemic patients	Not suggested in non-high-risk medical patients; suggested in high-risk medical patients; suggested for patients with postoperative acute respiratory failure	Not suggested in patients with established postextubation respiratory failure; suggested for patients with postoperative acute respiratory failure
HFNT	No data available in medical patients	Better than COT in unselected, non-high-risk medical patients; similar to NIV in high-risk medical patients; at least non-inferior to NIV in patients at risk of postoperative ARF after cardiothoracic surgery	No data available in medical patients; non-inferior to NIV in patients with postoperative ARF after cardiothoracic surgery

NIV=non-invasive ventilation. CPAP=continuous positive airway pressure. HFNT=high-flow nasal therapy. COT=conventional oxygen therapy. ARF=acute respiratory failure. *Based on the official ERS–ATS clinical practice guidelines on NIV for ARF and the ATS–ACCP clinical practice guidelines on liberation from mechanical ventilation in critically ill adults.[11,12]

Table 1: **Strategies of postextubation ventilatory support**

does not interfere with normal daily activities and results in higher compliance with treatment even in patients with claustrophobia who are intolerant to other devices.[65,66]

Oxygen

Oxygen is one of the most frequently administered therapies in the hospital setting. Supplemental oxygen therapy is prescribed to correct hypoxaemia and to prevent tissue hypoxia, preventing a switch to anaerobic metabolism, lactic acidosis, and ultimately cellular and tissue damage. COT is provided by easy-to-use devices, which are divided into low-flow devices (eg, nasal cannulae and simple face masks, with or without reservoirs) and high-flow devices (eg, the Venturi mask).[67] Low-flow nasal cannulas can be used at a maximum set O_2 flow of 4 L/min, above which discomfort related to airway dryness prevails, whereas a maximum O_2 flow of 15 L/min can be set with the Venturi mask or reservoir mask.[68] FiO_2 can be set more reliably with the Venturi mask, whereas it can only be estimated, on the basis of the set oxygen flow, with the other devices. With all conventional oxygenation devices, however, the real delivered FiO_2 will depend not only on the set oxygen flow but also on the patient's inspiratory flow, respiration rate, and tidal volume, which, at the highest values, can lead to entrainment of room air and reduction of delivered FiO_2.[69]

Ventilatory strategies to protect extubation in different patient populations

Liberating a patient from invasive mechanical ventilation is a daily challenge in the ICU. The planned extubation is a crucial moment whose timing is determined by resolution of the underlying cause of ARF and a successful spontaneous breathing trial. Even if the spontaneous breathing trial is successful, extubation can fail and might result in reintubation. Reintubation is associated with a greater risk of unfavourable outcome, leading to prolonged mechanical ventilation, a higher risk of ventilator-associated pneumonia, longer ICU and hospital stays, and increased mortality.[7] Implementing an appropriate strategy of postextubation ventilatory support can improve outcome.

Three strategies of ventilatory support can be used after extubation: facilitative, when it allows an early extubation in selected patients who have failed the spontaneous breathing trial, with the aim of reducing duration of invasive ventilation and its associated complications; preventive, in selected and unselected patients, to prevent onset of postextubation ARF; and therapeutic, to avoid reintubation in patients with postextubation ARF (figure 2, table 1).[70]

Facilitative strategy

Patients who have difficult weaning are exposed to complications related to prolonged invasive mechanical ventilation. In these patients, duration of the weaning phase can exceed 40–50% of the overall ventilation period.[71] Patients at higher risk of weaning failure often have been admitted with acute exacerbations of COPD, develop hypercapnia during the spontaneous breathing trial, or both. When these patients fail to meet extubation criteria after the spontaneous breathing trial, non-invasive ventilatory strategies for facilitative purpose allow early extubation, a shorter duration of invasive mechanical ventilation, and a faster weaning process. NIV is the only respiratory support that has been used for facilitative purposes after extubation in patients with COPD or with hypercapnia and several studies support its efficacy in this setting. The physiological rationale of this use of NIV was described by Vitacca and co-workers[32] in a study done in 12 patients affected by acute-on-chronic hypercapnic ARF, not able to sustain autonomous breathing. They showed that pressure support ventilation, delivered during invasive ventilation (before extubation) and during NIV (after extubation), produced the same effects in terms of gas exchange, diaphragmatic effort, and respiratory mechanics.[32] Furthermore, the dyspnoea score was substantially lower during NIV. The first clinical study on facilitative use of NIV during weaning was done by Nava and colleagues[72] in 50 patients with COPD and hypercapnic ARF, who were invasively ventilated for 48 h and had experienced failure of the first spontaneous breathing trial. These authors reported that early, continuous NIV, applied just after extubation as a bridge to unsupported spontaneous breathing, was able to reduce duration of mechanical

ventilation, ICU length of stay, ventilator-associated pneumonia, and 60-day mortality, as compared with conventional weaning done with invasive ventilation.[72] In 33 patients with acute-on-chronic respiratory failure, Girault and co-workers found that, when compared with a standard weaning approach, facilitative NIV yielded similar weaning success, survival, and ICU length of stay. NIV reduced time spent on invasive mechanical ventilation, although overall duration of mechanical ventilation increased.[73] Similar results were found in a subsequent, larger randomised controlled trial.[74] The clinical benefits of facilitative use of NIV were further supported in a small randomised controlled trial in patients with persistent weaning failure (ie, for 3 days). The trial was stopped after the first planned interim analysis (33 patients enrolled) because the NIV group showed a substantial reduction in duration of invasive ventilation, nosocomial acquired infections, tracheotomy, ICU stay, mortality, and other serious complications.[75] Burns and colleagues[76,77] have done several systematic reviews and meta-analyses, the last of which included 16 randomised controlled trials for a total of 994 patients, invasively ventilated for ARF from different causes (COPD, non-COPD, postoperative, medical) and weaned by means of early extubation followed by immediate application of NIV or invasive weaning. Most included patients had COPD exacerbations, eight trials included COPD exacerbations only, seven included a mix (but mostly COPD exacerbation), and one included hypoxaemic patients. They found that, compared with invasive weaning, weaning with NIV substantially decreased mortality, with greater benefits only in patients with COPD (risk ratio [RR] 0·36, 95% CI 0·24–0·56 in COPD *vs* RR 0·81, 95% CI 0·47–1·40 in mixed population). Furthermore, patients who received NIV had substantially shorter ICU stays, hospital stays, duration of invasive mechanical ventilation, and total duration of ventilation, and substantially less frequent weaning failure, ventilator-associated pneumonia, tracheotomy, and reintubation. Interpretation of these results should, however, take into account the limitations of the studies, which are mainly due to poor generalisability to different patient categories and the small number of patients included in each study.[76,77] One pilot trial (the one trial of hypoxaemia included in the Burns meta-analysis) has assessed the effects of NIV as a facilitative strategy for weaning in patients with hypoxaemic ARF.[78] After 48 h of invasive ventilation, 20 hypoxaemic patients were randomly assigned to standard weaning or to early extubation and NIV. There were no differences in gas exchange and likelihood of weaning success, but the number of days of invasive ventilation were substantially reduced in the NIV group. Although these results suggest the feasibility of facilitative NIV in selected hypoxaemic patients at experienced centres, the small number of patients precludes the drawing of any meaningful conclusion.

On the basis of the available evidence, the European Respiratory Society (ERS) and American Thoracic Society (ATS) guidelines suggested the use of NIV to facilitate weaning from mechanical ventilation in patients with hypercapnic ARF (conditional recommendation, moderate certainty of evidence), whereas no recommendation was provided for hypoxaemic patients.[11] No studies have assessed the effect of HFNT to facilitate weaning from mechanical ventilation. A post-hoc analysis[79] of the Bilevel Positive Airway Pressure Versus Optiflow study[80] suggested that facilitative HFNT or NIV had a similar effect on likelihood of treatment failure in patients who underwent cardiothoracic surgery (28% for HFNT *vs* 41% for NIV, respectively, p=0·33), but too few patients were included for any meaningful conclusion on this issue.

Preventive strategy

Respiratory support after extubation for preventive purposes aims to avoid postextubation ARF in patients undergoing planned extubation. Identifying patients at risk is important to select the most appropriate technique of respiratory support and to prevent extubation failure. Various risk factors for extubation failure have been described in the literature. They can be classified as risk factors related to the patient or comorbidities, risk factors related to acute pathology, and risk factors related to functional parameters, such as bedside predictive tests (panel).[1,3,4,7,81–88] The most commonly reported risk factors are older age (>65 years) and underlying cardiac or respiratory disease.[3,11] The patient's category (ie, medical or surgical) is also important, with extubation failure being more prevalent in critically ill medical patients (up to more than 20%) than in a surgical, postoperative setting (<10%).[90]

Critically ill medical patients

The effects of early application of NIV and HFNT soon after extubation, as an alternative to COT, have been assessed in unselected, non-high-risk patients (ie, any patients without risk factors after planned extubation) and in high-risk patients.

In unselected, non-high-risk patients, two studies did not show differences between preventive NIV and COT on reintubation frequency and mortality.[34,91] On the basis of these data, the ERS–ATS guidelines suggested not to use NIV to prevent postextubation ARF in this setting (conditional recommendation, very low certainty of evidence).[11]

Studies have highlighted the role of HFNT to prevent postextubation ARF. Maggiore and colleagues[9] did an open-label, bi-centre, randomised controlled trial to compare the effects of HFNT and COT (through a Venturi mask) applied immediately after extubation in 105 critically ill patients with moderate hypoxaemia (ie, arterial partial pressure of oxygen [PaO_2]/F_IO_2 ≤300) at the end of the spontaneous breathing trial preceding extubation. For the same delivered F_IO_2, patients treated with HFNT showed better oxygenation than those treated with the Venturi mask and this effect lasted up to 48 h.

***Panel*: Risk factors for extubation failure**

Factors related to patient and comorbidities

- Age >65 years[7,84,85]
- Moderate or severe cardiorespiratory disease[7]
- Body-mass index >30[89]

Factors related to acute pathology

- Neurological disease[82]
- Airway patency problem[85]
- Inability to deal with respiratory secretions[85]
- APACHE II >12 on extubation day[4,84]
- Difficult or prolonged weaning[85]
- ARF of cardiac origin[4]
- Pneumonia as the reason for intubation[81]
- Positive fluid balance[81]

Factors related to functional parameters

- Respiratory rate >35 breaths/min[1]
- Rapid shallow breathing index >105[88]
- MIP >−20 to −25 cm H_2O[1,82]
- Peak expiratory flow <60 L/min[86]
- $P_{0.1}$ ≤4·5 cm H_2O[82]
- VC ≤10 mL/kg[1,82]
- $P_{0.1}$/MIP <0·3[87]

APACHE II=Acute Physiologic Assessment and Chronic Health Evaluation II. ARF=acute respiratory failure. MIP= maximum inspiratory pressure. $P_{0.1}$=airway occlusion pressure at 0·1 s. VC=vital capacity.

Patients receiving HFNT also showed a reduction in respiratory rate and arterial partial pressure of carbon dioxide ($PaCO_2$), which was statistically significant at 3 h after extubation. In addition, patients experienced less discomfort, fewer displacements of the interface, and fewer desaturations with HFNT. Finally, fewer patients had postextubation ARF requiring any form of ventilator support (8% for HFNT *vs* 35% for Venturi mask, p<0·001), NIV (4% *vs* 15%, p=0·042), or reintubation (4% *vs* 21%, p=0·005) in the HFNT group, suggesting a potential role of this technique in preventing extubation failure. The benefit of HFNT in reducing reintubation was observed mainly in patients reintubated because of hypoxaemia or inability to clear secretions.[9] Hernàndez and co-workers did a multicentre randomised controlled trial to assess the effects of 24 h of HFNT and COT in preventing reintubation in 527 mechanically ventilated patients (medical and surgical) at low risk for extubation failure.[89] In line with the results of Maggiore and colleagues,[9] they found that use of HFNT was associated with a reduction in the proportion of patients needing reintubation at 72 h (5% *vs* 12%, p=0·004), in the frequency of postextubation ARF (8% *vs* 14%, p=0·03), and in laryngeal oedemas requiring intubation (0% *vs* 3%, p=0·001), whereas time to reintubation was similar in both groups.[89] A meta-analysis of seven studies including the two aforementioned studies showed that HFNT significantly decreased the reintubation frequency compared with COT in 632 critically ill medical patients (RR 0·35, 95% CI 0·19–0·64; p=0·0007).[92] In summary, HFNT can be an attractive and more effective approach than COT to prevent postextubation ARF in unselected ICU patients.

Several studies have assessed the effects of preventive NIV in high-risk ICU patients. Nava and co-workers[85] did the first multicentre randomised controlled trial to evaluate whether, as compared with COT and standard medical therapy, the early application of NIV immediately after extubation was effective in preventing postextubation ARF in high-risk, critically ill patients. In Nava and co-workers' study, high-risk critically ill patients were defined by the following criteria: more than one consecutive failure of the weaning trial, chronic heart failure, $PaCO_2$ greater than 45 mm Hg after extubation, more than one comorbidity (excluding chronic heart failure), weak cough defined as an airway care score greater than 8 and less than 12, or upper airways stridor at extubation not requiring immediate reintubation. The panel includes the most common risk factors reported in literature, including these ones (also with different terminology). The authors reported a significant reduction of reintubation frequency (4 [8%] of 48 for NIV *vs* 12 [24%] of 49 for COT, p=0·03), which in turn was associated with a lower ICU mortality, in the NIV group. In a subsequent study of 162 patients by Ferrer and colleagues, no difference in reintubation frequency was found between NIV and COT delivered through a Venturi mask in patients at risk of postextubation ARF.[84] A reduction in postextubation ARF (16% for NIV *vs* 33% for COT, p=0·03) and in ICU mortality (3% *vs* 14%, p=0·015) was observed with NIV, although hospital mortality and 90-day survival were similar. In patients with hypercapnia during the spontaneous breathing trial, NIV was associated with a significant reduction in ICU and hospital mortality and an increase in 90-day survival.[84] The same authors repeated these results in a randomised controlled trial of 106 patients with chronic respiratory disorders developing hypercapnia during the spontaneous breathing trial.[93] The frequency of postextubation ARF was lower in the NIV group than in controls (15% *vs* 48%, p<0·0001). In addition, 90-day survival was significantly improved with NIV. In a before-and-after study, Thille and colleagues found that implementation of a preventive NIV protocol significantly reduced the risk of reintubation in patients at risk of extubation failure (23 [15%] of 150 *vs* 23 [28%] of 83, p=0·02).[94] In the control cohort, composed of patients treated before implementation of preventive NIV protocol, no patient received preventive NIV, they received COT. On the basis of the available data, the ERS–ATS guidelines suggested that NIV should be used to prevent postextubation ARF in high-risk patients (ie, >65 years old or those with underlying cardiac or respiratory disease; conditional recommendation, low certainty of evidence.[11] The same recommendation was made by the American College of Chest Physicians–ATS clinical practice guideline on liberation from mechanical

ventilation in critically ill adults (strong recommendation, moderate certainty of evidence).[12,95]

Only one study compared HFNT and NIV in critically ill patients at risk of extubation failure. Hernàndez and co-workers did a multicentre, non-inferiority randomised controlled trial in 604 high-risk patients, comparing preventive use of HFNT or NIV, applied soon after extubation and maintained for 24 h.[83] HFNT was not inferior to NIV in preventing reintubation (19·1% for NIV *vs* 22·8% for HFNT; absolute risk difference −3·7; 95% CI −9·1 to ∞; in the multivariable analysis, the marginal odds ratio (OR) was 1·25; 95% CI 0 to 1·74), despite the postextubation ARF frequency at 72 h being higher in the NIV group (39·8% for NIV *vs* 26·9% for HFNT; absolute risk difference 12·9; 95% CI 6·6 to ∞), probably because of greater patient discomfort and difficulties in optimising NIV application; this possibility is also suggested by the shorter-than-planned duration of NIV in the NIV group (14 h, instead of 24 h as intended in the study protocol). As compared with NIV, HFNT is advantaged by its ease of use and the lower skill and expertise required by the operators. The results of this trial support previous findings that HFNT is very well tolerated,[9,96] which in turn might facilitate its application and could increase patient compliance with treatment. The trial also indicated that HFNT can be an effective alternative to NIV for preventing ARF in high-risk patients, although further investigation is needed.

Postoperative setting

Because postoperative ARF increases reintubation frequency, morbidity, mortality, and length of hospital stay,[97,98] preoperative risk scores have been developed to identify patients at risk (ie, those who are older or with obesity, COPD, or heart disease) and to apply preventive, perioperative support strategies.[99]

Several studies have specifically evaluated the application of CPAP and NIV in the postoperative period for patients undergoing major surgery under a general anaesthetic. The ERS–ATS guidelines suggested NIV for patients with postoperative ARF (conditional recommendation, moderate certainty of evidence), without differentiating, however, between prophylactic or therapeutic use of NIV.[11] Chiumello and colleagues[100] did a systematic review on the use of NIV and CPAP for preventive and therapeutic purposes after various types of major surgery (abdominal, thoracic, thoraco-abdominal vascular, cardiac, and bariatric surgery). They found that, as compared with COT, either preventive NIV or CPAP in the postoperative period improved lung volumes and gas exchange and might decrease pulmonary complications, reintubations, and hospital length of stay. In a multicentre randomised controlled trial, Squadrone and colleagues assessed the effects of CPAP versus COT in 209 patients developing hypoxaemia within 1 h after abdominal surgery.[101] The early use of CPAP, effectively as a preventive strategy, decreased frequency of reintubation (1% *vs* 10%, p=0·005), as well as pneumonia (2% *vs* 10%; p=0·02) and sepsis (2% *vs* 9%; p=0·03).

Few trials have assessed the effects of HFNT and COT in preventing postoperative ARF in patients who have undergone cardiac or thoracic surgery.[63,102–105] These studies reported conflicting results in terms of the effect of HFNT on atelectasis and oxygenation. One study, done in 340 patients who had undergone cardiac surgery, found that escalation in respiratory support owing to ARF onset was lower with HFNT (38% for HFNT *vs* 62% for COT).[102] Two other studies done after thoracic surgery reported that HFNT decreased reintubations or hospital length of stay.[103,104] These three studies, however, were not powered for these outcomes. The Bilevel Positive Airway Pressure Versus Optiflow study was the first, large, multicentre randomised controlled trial in this area, comparing HFNT and NIV in 830 patients who had undergone cardiothoracic surgery and developed hypoxaemia during the spontaneous breathing trial or after extubation.[80] In this non-inferiority trial, NIV and HFNT were applied according to three different strategies: facilitative, preventive, or curative. Treatment failure, defined as reintubation, switch to the other treatment, or premature discontinuation, was similar in both groups (21% for HFNT and 21·9% for NIV, for the three strategies combined; absolute risk difference 0·9%, 95% CI −4·9% to 6·6%, p=0·003), as were reintubations (14% in both groups). A post-hoc analysis showed that there were no differences in the proportion of patients with treatment failure between HFNT and NIV when these techniques were used as a facilitative strategy or as a curative strategy.[79] When considered as preventive strategies, however, treatment failure was lower in the HFNT group (6%) than in the NIV group (13%; p=0·04). Futier and colleagues evaluated the clinical efficacy of HFNT and COT after extubation in 220 patients at medium-to-high risk (Assess Respiratory Risk in Surgical Patients in Catalonia risk score of ≥26 points) of postoperative pulmonary complications after major abdominal surgery (OPERA trial).[106] No difference was found between the two groups in the proportion of patients with hypoxaemia (PaO_2/FiO_2 ≤300) at 1 h after extubation and at treatment discontinuation. Postoperative pulmonary complications, duration of hospital stay, and hospital mortality were also similar between groups. Given the paucity of data available in patients undergoing major abdominal surgery and the results of the OPERA trial, the potential usefulness of HFNT after extubation in these patients remains unclear.

Therapeutic strategy

Therapeutic strategies of ventilatory support are applied in cases of postextubation ARF, with the aim of avoiding reintubation both in critically ill medical patients and in the postoperative setting.

Critically ill medical patients

The ERS–ATS guidelines suggested that NIV should not be used in the treatment of medical patients with

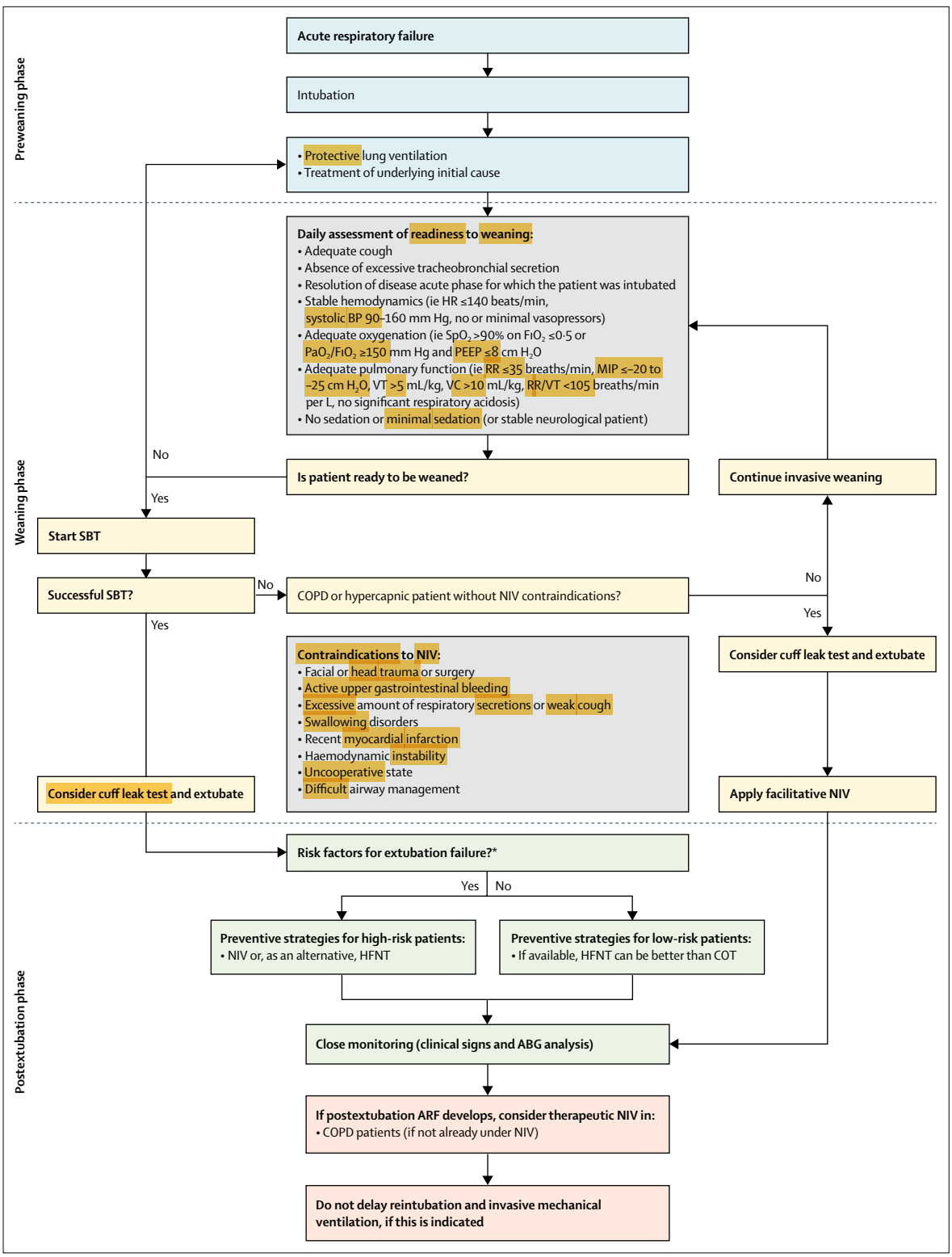

Figure 3: **Algorithm for ventilatory support after extubation in critically ill medical patients**

HR=heart rate. BP=blood pressure. SpO_2=pulse-oximeter oxygen saturation. FiO_2=fraction of inspired oxygen. PaO_2=arterial partial pressure of oxygen. RR=respiratory rate. MIP=maximal inspiratory pressure. VT=tidal volume. VC=vital capacity. SBT=spontaneous breathing trial. COPD=chronic obstructive pulmonary disease. NIV=non-invasive ventilation. HFNT=high-flow nasal therapy. COT=conventional oxygen therapy. ABG=arterial blood gas. ARF=acute respiratory failure. * See panel.

established postextubation ARF (conditional recommendation, low certainty of evidence).[11] This suggestion was based on the results of two randomised controlled trials comparing the effects of NIV and COT on clinical outcome.[8,107] In a single-centre randomised controlled trial, Keenan and colleagues[107] randomly assigned 81 high-risk patients with postextubation respiratory distress to NIV or COT and found no difference in the proportion needing reintubation (72% *vs* 69%; RR 1·04, 95% CI 0·78–1·38) or hospital mortality (31% for both groups RR 0·99, 95% CI 0·52–1·91).[107] Esteban and colleagues did a multicentre randomised controlled trial to evaluate the effect of NIV versus COT on all-cause mortality in 221 patients with postextubation ARF.[8] No differences were found in reintubation frequency and ICU length of stay. In the NIV group, however, ICU all-cause mortality was higher (25% *vs* 14%; RR 1·78, 95% CI 1·03–3·20, p=0·048) and the time between onset of respiratory distress and reintubation was longer in the NIV group (median, 12 h, IQR, 2 h 10 min–28 h) than in the standard-therapy group (median, 2 h 30 min, IQR, 45 min–16 h 30 min, p=0·02; RR and CI not indicated for this outcome), suggesting that delay in reintubation might worsen outcomes. Of note, these two trials enrolled few patients with COPD who had postextubation ARF, and therefore their results cannot apply to this condition.

To our knowledge, no data on the therapeutic use of HFNT in critically ill medical patients is available to date.

Postoperative setting

By contrast with medical patients, the ERS–ATS guidelines suggested NIV for patients with postoperative ARF (conditional recommendation, moderate certainty of evidence) for therapeutic purposes.[11] Chiumello and colleagues reported that, as compared with COT, therapeutic NIV and CPAP in the postoperative period improved atelectasis and gas exchange and might decrease reintubations, mortality, ICU length of stay, and complications.[100] In particular, studies have shown that therapeutic NIV can improve outcomes after thoracic and abdominal surgery and in patients undergoing solid organ transplantation.[101,108–111] Auriant and colleagues[109] reported that, as compared with COT, NIV could reduce the need for reintubation (21% *vs* 50%; p=0·035) and hospital mortality (13% *vs* 38%; p=0·045) in 48 patients developing ARF after lung resection. Jaber and colleagues[111] did a multicentre randomised controlled trial comparing NIV and COT in 293 patients developing postoperative ARF following abdominal surgery. NIV decreased the proportion of patients with reintubation occurring within 7 days (33% *vs* 46%; p=0·03) and healthcare-associated infections (31% *vs* 49%; p=0·003). In 40 patients with postoperative ARF after solid organ transplantation, Antonelli and colleagues found that NIV, as compared with COT, improved oxygenation and decreased the need for reintubation (20% *vs* 70%; p=0·002), frequency of complications, and ICU mortality.[108]

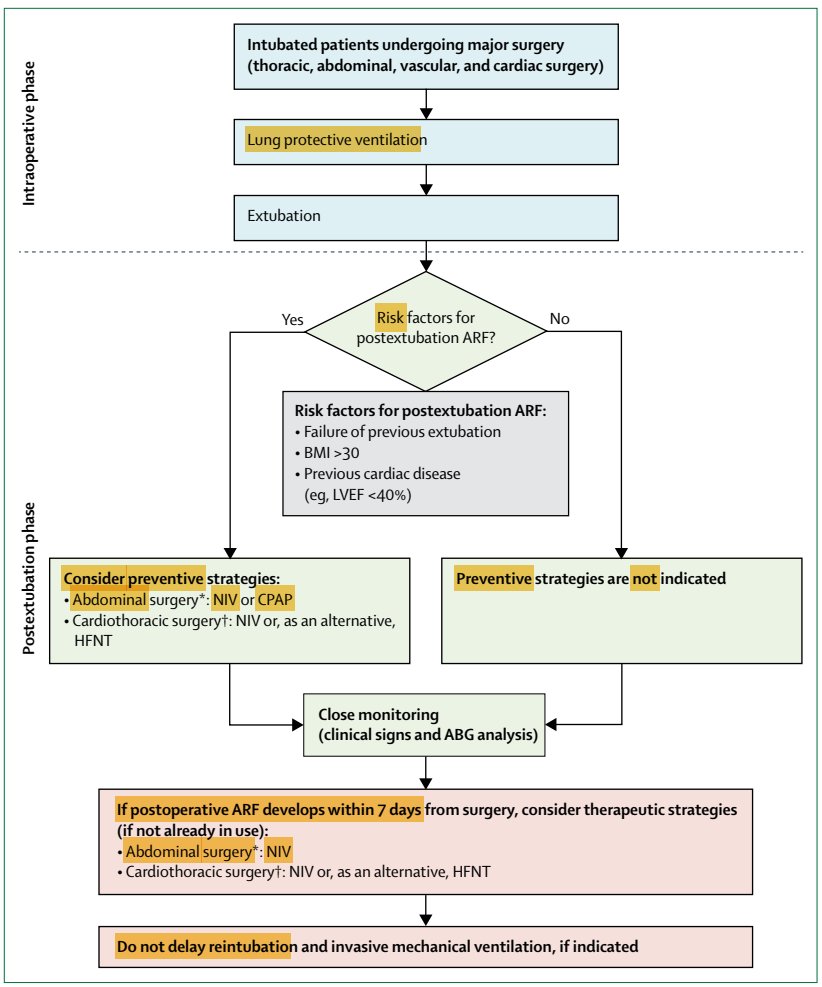

Figure 4: **Algorithm for ventilatory support after extubation in postoperative setting**
ARF=acute respiratory failure. BMI=body mass index. LVEF=left ventricular ejection fraction. NIV=non-invasive ventilation. CPAP=continuous positive airway pressure. HFNT=high-flow nasal therapy. ABG=arterial blood gas. * Abdominal surgery includes abdominal vascular surgery. †Cardiothoracic surgery includes thoracic vascular surgery.

In patients developing ARF after cardiothoracic surgery, HFNT and NIV are equally effective in avoiding reintubation when used for therapeutic purposes.[80] A post-hoc analysis[79] of the Bilevel Positive Airway Pressure Versus Optiflow non-inferiority trial[80] showed, in fact, that there were no differences in treatment failure between the two techniques, when used in the context of a therapeutic strategy (27% for HFNT vs 28% for NIV, p=0·93). This might suggest that postoperative HFNT can be used as a first-line, non-invasive technique of respiratory support after cardiothoracic surgery because it is non-inferior to NIV overall, could even decrease the likelihood of treatment failure in some patients when used as a preventive strategy, and provides some advantages over NIV, such as ease of application.

Clinical implications

Weaning from mechanical ventilation is a complex process that should start as early as possible,

theoretically soon after the beginning of mechanical ventilation, and continues up to the time when a possible postextubation ARF occurs and must be managed (figure 2). The first step is, therefore, represented by an appropriate management of invasive mechanical ventilation based on lung protection. This prerequisite is valid both for critically ill medical patients and for patients undergoing a surgical procedure, in which potential lung injury due to non-protective, intraoperative mechanical ventilation is often underestimated.[112] Lung injury can result in a longer invasive ventilation and in a higher risk of difficult weaning and postextubation ARF compared with patients without lung injury.[112]

After extubation, available strategies of respiratory support should be chosen based on the type of patient (medical or surgical), the level of risk of postextubation ARF, and the cause of ARF (table 1, figures 3 and 4). Table 2 lists suggested settings for different techniques of ventilatory support after extubation.

Critically ill medical patients should undergo a daily assessment of their ability to breathe unassisted to evaluate as early as possible the possibility of extubation.[1] At this stage, it is also important to assess whether the patient has risk factors for extubation failure (panel). In selected categories of patients, such as those with COPD or developing hypercapnia during the spontaneous breathing trial, early extubation and facilitative NIV should be considered even after failure of the spontaneous breathing trial, if some degree of recovery from the initial cause of ARF has been achieved (ie, after 48 h) and no contraindication to NIV exists (figure 3).[11,72,74] After a successful spontaneous breathing trial, strategies differ according to risk of extubation failure. If no risk factor has been identified (low-risk patients), HFNT is the preferable preventive strategy if the device is available, given the advantages over COT (figure 3).[9,89,92] In high-risk patients, NIV might prevent postextubation ARF compared with COT.[11] This protective effect is greater in hypercapnic patients and those with COPD exacerbation or heart failure compared to non-hypercapnic patients, non-COPD patients, and patients without heart failure,[84,93] whereas the use of NIV is debated in patients with hypoxaemic ARF.[11] Preventive NIV should be started immediately after extubation and applied continuously for at least the first 24 h. In high-risk patients, HFNT can be used as an alternative to NIV, because it is not inferior to NIV in preventing postextubation ARF and is associated with better patient comfort and greater ease of use. Besides the availability of devices, the choice of NIV or HFNT in these patients depends on personnel skill and expertise with these techniques (figure 3).[83] If postextubation ARF develops, NIV is not recommended as a curative strategy in medical patients and intubation should be preferred. In selected patients with COPD, however, a trial of NIV could be considered, if applied in a safe environment (figure 3).[11]

In the postoperative setting, preventive strategies should be considered in case of a high risk of postextubation ARF. Different options exist according to the type of surgery. After abdominal and abdominal vascular surgery, early NIV or CPAP are beneficial.[101,111] After cardiothoracic surgery, including thoracic vascular surgery, NIV is also useful.[11] In these patients, HFNT can be used as an alternative to NIV; it has similar effects on outcome and can be easier to use (figure 4).[11,80] If postextubation ARF develops within 7 days from surgery, provided that surgical complications are excluded and the patient is cooperative and able to protect their airway, NIV should be considered in patients who have undergone abdominal or cardiothoracic surgery.[11,109,111] In cardiothoracic surgery, HFNT can be used as an alternative to NIV (figure 4).[11,80]

In any case, in both medical and surgical patients, the use of any technique of postextubation respiratory support should not delay intubation and escalation to invasive mechanical ventilation when this is more appropriate, because delay can worsen the patient's outcome and increase mortality (figures 3 and 4).[8,113,114]

	NIV	CPAP	HFNT
Settings	Ventilatory mode: pressure support ventilation; PSV level: 5–15 cm H_2O; PEEP: 4–5 cm H_2O, up to 8–10 cm H_2O; Inspiratory trigger sensitivity: as high as possible while avoiding autotriggering (eg, flow trigger 1–2 L/min); pressurisation ramp: high (eg, 80% on a scale 0–100%); expiratory trigger: 25–30% (up to 50–60% in patients with any chronic obstructive pathology with increased time constant and dynamic hyperinflation; FiO_2: the lowest to reach the SpO_2 target	PEEP: 5–10 cm H_2O; Total gas flow: ≥30 L/min, to avoid rebreathing; FiO_2: the lowest to reach the SpO_2 target	Gas flow: 30–60 L/min, according to patient comfort; gas temperature: 31–37°C, according to patient comfort and gas flow (higher temperature with higher gas flow); FiO_2: the lowest to reach the SpO_2 target
Targets	Tidal volume: 6–8 mL/kg predicted body weight; respiratory rate ≤30 breaths/min; SpO_2: 92–98% or 88–92% in patients with chronic respiratory disease	Respiratory rate ≤30 breaths/min; SpO_2: 92–98% or 88–92% in patients with chronic respiratory disease	Respiratory rate ≤30 breaths/min; SpO_2: 92–98% or 88–92% in patients with chronic respiratory disease

NIV=non-invasive ventilation. CPAP=continuous positive airway pressure. HFNT= high-flow nasal therapy. PSV=pressure support ventilation. PEEP=positive end-expiratory pressure. FiO_2=inspired oxygen fraction. SpO_2=pulse-oximeter oxygen saturation.

Table 2: **Suggested starting settings for NIV, CPAP, and HFNT after extubation**

	Study title (abbreviation)	Design	Intervention	Primary outcome
NCT02107183	Impact of nasal high-flow *vs* Venturi mask oxygen therapy on weaning outcome: a multicenter, randomized, controlled trial (RINO)	Interventional, phase not applicable; projected n=500	Optiflow (Fisher & Paykel Healthcare) *vs* Venturi mask	Reintubation within 72 h after extubation or at ICU discharge
NCT03246893	Efficacy of HFNC *vs* NIV for preventing reintubation in sepsis patients	Interventional, phase not applicable; projected n=210	Non-invasive positive pressure ventilation *vs* high-flow oxygen nasal cannula	Device failure rate
NCT03361683	Postextubation high-flow nasal oxygen for preventing extubation failure	Interventional, phase not applicable; projected n=170	High-flow nasal oxygen *vs* Venturi mask	Postextubation failure
NCT03495947	HFNC in immediately post extubation	Observational; projected n=150	HFNC	Extubation failure
NCT02290548	Effect of high-flow nasal oxygen on extubation outcome	Interventional, phase not applicable; projected n=400	HFNC immediately used after extubation *vs* standard oxygen therapy	Reintubation rate
NCT03441854	HFNC *vs* conventional oxygen therapy after extubation in liver transplantation	Observational; projected n=30	HFNC oxygen delivery after extubation *vs* Venturi mask	Post-operative oxygenation measured at 1 h after extubation
NCT01928238	Physiological effects of non-invasive neurally adjusted ventilatory assist (NAVA) *vs* noninvasive pressure support ventilation in patients at risk for respiratory distress needed preventive use of non-invasive ventilation after extubation (NIV-NAVA)	Interventional, phase not applicable; projected n=13	Non-invasive neurally adjusted ventilatory assist (NIV-NAVA) *vs* non-invasive pressure support ventilation (NPSV)	Inspiratory muscle effort
NCT03288311	Protocolised postextubation respiratory support study (PROPER)	Interventional, phase not applicable; projected n=630	Protocolised postextubation respiratory support *vs* usual care	Rate of reintubation within the 96 h after extubation
NCT03562000	Preventing extubation failure related to cough (PREXFAIL)	Interventional, phase 3; projected n=368	Cough assistance and systematic non-invasive ventilation	Reintubation rate, including every cause
NCT01967108	Postextubation chest physiotherapy in ICU	Interventional, phase not applicable; projected n=65	Chest physiotherapy	Rate of reintubation within the 48 h after extubation

HFNC=high-flow nasal cannula. ICU=intensive care unit.

Table 3: **Ongoing studies on respiratory support after extubation (from ClinicalTrials.gov)**

Areas of uncertainty and future research

There are several areas of uncertainty concerning the use of ventilatory support after extubation. How to individually tailor treatment to protect extubation is not clear, a relevant issue in the era of precision medicine and personalisation of care. The variability in inclusion and exclusion criteria creates considerable heterogeneity among published studies. We need, therefore, to better characterise patients at risk of extubation failure, which implies a better definition of risk factors for postextubation ARF. Understanding the mechanistic linkage between causes and symptoms of postextubation ARF would allow improved selection of treatments for individual patients. Data suggest that the choice of interface, such as helmets versus masks, could affect outcome of NIV.[115] Assessing the role of different NIV interfaces and emerging technologies such as HFNT or extracorporeal gas exchange will certainly be areas of future research. Treatment dose, timing, and intensity for both established practices (NIV, CPAP) and new techniques (eg, HFNT) are also areas where research is needed. The value of different postextubation ventilatory strategies (facilitative, preventive, and therapeutic) is not fully elucidated, especially for specific categories of patients such as those without hypercapnia, and will need further investigation, as will other technologies such as electrical pacing of the

Search strategy and selection criteria

We used our existing knowledge of publications on the subject and identified additional references for this Review through searches of PubMed for articles published from Jan 1, 1970, to April 30, 2018, using the search terms "noninvasive ventilation", "continuous positive airway pressure", "high-flow nasal cannula", "nasal high-flow", "nasal high-flow oxygen", "oxygen therapy", "extubation", "weaning", and "acute respiratory failure", with different combinations. The search was limited to studies done in adult humans (≥18 years old). We reviewed articles resulting from these searches and references cited in those articles and we selected the relevant ones. We included articles published in English, French, Italian, Spanish, and German.

diaphragm by transvenous phrenic nerve stimulation to reduce diaphragm dysfunction.[116] Finally, early physiotherapy could play an important part in the weaning process.[117] Research in these areas is ongoing and could contribute to improvement of weaning outcome (table 3).

Conclusions

Non-invasive ventilatory support after extubation has an important role in improving the outcome of weaning from invasive mechanical ventilation. Several techniques are available nowadays and others are emerging. These techniques are incorporated in different strategies to facilitate extubation, and to prevent or to treat post-extubation ARF. Guidelines should direct the implementation of NIV strategies in everyday clinical practice. In some areas, research is ongoing and additional evidence is needed. For instance, it will be important to precisely define the risk factors for extubation failure, the relative value of NIV and HFNT, and the dose, timing, and duration of postextubation respiratory support to help clinicians to use the right device, with the right setting, in the right patient, at the right time.

Contributors

SMM conceived the idea for this Review. MB and SMM contributed to the literature search and developed the first draft. LS, MB and SMM prepared the figures. SMM and FP revised and finalised the manuscript and the figures. All authors contributed to and approved the final version of the report.

Declaration of interests

We declare no competing interests.

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